

The Claims

This listing of claims will replace all prior versions and listings of all claims in the application.

1-16. (Canceled)

17. **(Currently Amended)** A mixed TNFSF oligomer comprising:

a) one or two non-wild-type variant monomer(s) of a Tumor Necrosis Factor Super Family ("TNFSF") protein comprising at least a variant extracellular domain of said TNFSF monomer protein, wherein said variant TNFSF protein comprises an amino acid sequence that has at least one amino acid substitution in the Large Domain and at least one amino acid substitution in a domain selected from the group consisting of the DE Loop and the Small Domain; and,

b) one or two wild-type TNFSF monomer(s) of said corresponding TNFSF protein; wherein said mixed TNFSF oligomer is substantially incapable of activating receptor signaling in all cognate receptors ~~has at least a 50% decrease in receptor activation as~~ compared to a homotrimer of said wild-type TNFSF oligomer.

18. **(Currently Amended)** A non-wild-type variant Tumor Necrosis Factor Super Family ("TNFSF") protein as compared to a wild-type TNFSF protein, comprising at least a variant extracellular domain of said TNFSF protein, wherein said variant TNFSF protein will interact *in vivo* with said corresponding wild-type TNFSF oligomer to form a mixed TNFSF oligomer, wherein said variant TNFSF protein comprises an amino acid sequence that has at least one amino acid substitution in the Large Domain and at least one amino acid substitution in a domain selected from the group consisting of the DE Loop and the Small Domain, and wherein said mixed TNFSF oligomer is substantially incapable of causing receptor activation in all cognate receptors as compared to a homotrimer of said wild-type TNFSF oligomer.

19. (Canceled)

20. (Original) A variant TNFSF protein according to claim 18 comprising at least one receptor contact domain that has reduced affinity for a desired receptor as compared to its corresponding wild-type TNFSF protein and retains the ability to interact with other receptor interaction domains.

21. (Canceled)

22. (Previously Presented) A variant TNFSF protein according to claim 18, wherein said variant TNFSF protein physically interacts with a wild-type TNFSF protein to form mixed trimers.

23. (Original) A mixed TNFSF oligomer comprising at least one variant TNFSF protein monomer according to claim 18 comprising a substitution at a receptor contact position.

24. (Original) A variant TNFSF monomer protein according to claim 18, wherein said variant TNFSF protein comprises a substitution at a trimer interface position.

25. (Previously Presented) A variant TNFSF protein according to claim 18, wherein said variant TNFSF protein physically interacts with its corresponding wild-type TNFSF protein.

26-35. (Canceled)

36. (Previously Presented) A variant TNFSF protein according to claim 17, wherein at least one substitution is non-conservative.

37. (Previously Presented) A variant TNFSF protein according to claim 17, wherein at least one substitution is a surface substitution.

38. (Cancelled)

39. (**Currently Amended**) A variant TNFSF protein according to claim 18~~[[38]]~~, wherein at least one of said Large Domain substitutions is at a position selected from the group consisting of TNF- α (SEQ ID NO:1) corresponding positions 28, 29, 30, 31, 32, 33, 34, 63, 64, 65, 66, 67, 68, 69, 112, 113, 114, 115, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146 and 147.

40. **(Currently Amended)** A variant TNFSF protein according to claim ~~18~~³⁸, wherein at least one of said Small Domain substitutions is at a position selected from the group consisting of TNF- α (SEQ ID NO:1) corresponding positions 72, 73, 74, 75, 76, 77, 78, 79, 95, 96, 97 and 98.

41. **(Currently Amended)** A variant TNFSF protein according to claim ~~18~~³⁸, wherein at least one of said DE Loop substitutions is at a position selected from the group consisting of TNF- α (SEQ ID NO:1) corresponding positions 84, 85, 86, 87, 88 and 89.

42. **(Currently Amended)** A variant TNFSF protein according to claim ~~18~~³⁸, wherein at least one of said Trimer interface substitutions is at a position selected from the group consisting of TNF- α (SEQ ID NO:1) corresponding positions 11, 13, 15, 34, 36, 53, 54, 55, 57, 59, 61, 63, 72, 73, 75, 77, 119, 87, 91, 92, 93, 94, 95, 96, 97, 98, 99, 102, 103, 104, 109, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 147, 148, 149, 151, 155, 156 and 157.

43. (Original) A variant TNFSF protein according to claim 42, wherein at least one of said Trimer interface substitutions is at a position selected from the group consisting of: 57, 34, and 91.

44. (Previously Presented) A variant TNFSF protein according to claim 18, wherein said variant TNFSF protein antagonizes soluble wild-type TNFSF proteins.

45. **(Currently Amended)** A pharmaceutical composition comprising a variant TNFSF protein according to any of claims 17, 18, 20 and 22-~~25~~⁴⁶ and a pharmaceutically acceptable carrier.